Studies on bioactive molecules from neem leaf extract and their mechanism of action against gastric ulcer

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Abstract

The neem (*Azadirachta indica*) is a evergreen tree generally found in India, Africa, Central America, South America, North America and Australia. The ancient Indian found many therapeutic uses for the neem leaves and leaves extract have been demonstrated as anti-inflammatory, anti-mutagenic, anti-carcinogenic, chemotherapeutic and hypoglycaemic properties. Moreover, The extract has also reported to prevent different human diseases like, cancer (e.g. prostate cancer. Brest cancer, human leukemia cancer cell) and sepsii diseases. The different parts of neem e.g. leaves, seeds, bark, flowers, fruits and roots exhibit various medicinal properties and biological activities. More than 200 compounds are isolated from different parts of neem while more than 60 compounds are isolated from neem leaves. Considerable knowledge has been gathered on the damaging role of acid and oxidative damage by reactive oxygen species (ROS) in all types of gastric ulcer. Several factors such as excess use of nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, infection by *Helicobacter pylori* and stress remain major reasons for gastric ulcer development. One of the major cause of gastric ulcer is uncontrolled secretion of hydrochloric acid into the gastric lumen from the parietal cells of the gastric mucosa through the proton-pumping by H^+-K^+-ATPase. In addition, degradation of extracellular matrix (ECM) of gastric tissue has been documented as other major reason. Matrix metalloproteinases (MMPs) are a diverse family of enzymes capable of degrading various components of the ECM. The MMPs are synthesized as inactive zymogen (pro-MMPs) and activated by ROS and other proteases by removal of the propeptide domain. The role of antioxidants for gastric ulcer prevention as well healing is well accepted, however the influence of antioxidants on the activity of MMPs is not known clearly. The possibility has strongly supported by previous studies from our and other laboratories on the action of antioxidants (e.g. curcumin, melatonin and quercetin) in regulating MMP-9 activity during prevention of gastric ulcers. In this thesis the efficacy of crude methanolic neem leaves extract in comparison with aqueous extract of neem leaves during gastroprotection on indomethacin-induced murine gastric ulcer model was investigated. Secondly, we wanted to isolate and characterize the lead molecule from crude methanolic extract of neem leaves that possess the gastroprotective property. Finally, the study focuses on the mode of action of lead compound from neem leaf that target matrix metalloproteinase-9 biochemical pathway during gastric ulcer prevention.

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